

REMARKS

Reconsideration and withdrawal of the objections to and rejections of the application are respectfully requested in view of the amendments, remarks and enclosures herewith, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 20-27, 29, 30 and 44 are pending in this application. New claim 44 is currently added without prejudice, without admission, without surrender of subject matter and without any intention of creating any estoppel as to equivalents.

Claim 20 has been amended to recite an isolated equine GM-CSF polypeptide of equine or synthetic origin which has an adjuvant effect, immunity stimulant activity, and species specificity as that of equine GM-CSF as set forth in SEQ ID NO:9. Claim 20 is supported throughout the present application, including by the text at page 2, lines 5-10 (describing that GM-CSF has an adjuvant effect, stimulates haematopoietic cells and increases immune response); page 3, line 29 to page 4, line 8 (describing that invention includes polypeptides of equine origin or which are synthetic having substantially equivalent activity to that of natural equine GM-CSF); and page 4, lines 11-34 (describing invention as including expression vectors transformed by a sequence according to the invention, and equine GM-CSF proteins thus produced and their use as an adjuvant for vaccines or for stimulating immunity). No new matter is added.

Claims 21-27, 29, and 30 have been amended to parallel the language used in claim 20, with claim 22 in independent form as suggested in the Office Action. The support for claim 20 also provides support for the amendments to claims 21-27, 29 and 30; and, see also support throughout the application, including the text at page 2, line 33 to page 3, line 7 (describing invention as covering equivalent nucleic acid sequences to SEQ ID NO:8, e.g., which differ by the degeneracy of the genetic code, or having 90% or 92% or 95% identity with SEQ ID NO:8, and encode a protein of equivalent functionality and specificity in horses to equine GM-CSF of the invention, e.g., SEQ ID NO:9), and page 3, lines 21-25 (describing invention as including equine GM-CSF polypeptide encoded by SEQ ID NO:8 or equivalent sequences).

New claim 44 parallels claim 22, but involves the polypeptide having SEQ ID NO:9 (i.e., claim 44 is in independent form as suggested for claim 22, but if claim 44 was dependent, it would depend upon claim 21, whereas claim 22 previously depended upon claim 20). Claim 44 is supported by that which supports the amendments for claims 20-27, 29 and 30, including the

support for the now pending throughout the application, and including the text at page 2, line 33 to page 3, line 7 (describing invention as covering equivalent nucleic acid sequences to SEQ ID NO:8, e.g., which differ by the degeneracy of the genetic code, and encode a protein of equivalent functionality and specificity in horses to equine GM-CSF of the invention, e.g., SEQ ID NO:9) and page 3, lines 21-25 (describing invention as including equine GM-CSF polypeptide encoded by SEQ ID NO:8 or equivalent sequences).

No new matter is added. Furthermore, the non-statutory objection to claims 22 and 23 are overcome by claim 22 being in independent form. (And it is otherwise noted that claim 22 and the claims dependent thereon and claim 44 were and are proper product-by-process claims.) Thus, reconsideration and withdrawal of the objection to claims 22 and 23 are respectfully requested.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art, and that the claims previously presented were in full compliance with the requirements of 35 U.S.C. § 112, and that the claims as presented herein are in full compliance with the requirements for patentability within 35 U.S.C. §§§§ 101, 102, 103 or 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply to round out the scope of protection to which Applicants are entitled; and, the amendments herein are not considered to give rise to any prosecution history estoppel.

II. THE OBJECTIONS TO THE SPECIFICATION ARE OVERCOME

The disclosure was objected to because the status of the application to which the instant application claims priority was not updated. Furthermore, the Abstract of the disclosure was objected to because it should be a single paragraph whereas it was followed by "Figure 1".

The specification has been amended to reflect the status of the applications to which the application claims priority. Moreover, the Abstract of the disclosure has been amended to eliminate the recitation "Figure 1" following the Abstract. The text of the Abstract has also been replaced with the text headed "**ABSTRACT OF THE DISCLOSURE**" submitted herewith on a separate sheet at the end of this paper.

No new matter is added by these amendments.

Applicants respectfully submit that the amendments herewith overcome the objections to the specification. Consequently, reconsideration and withdrawal of the objection to the specification is respectfully requested.

III. THE SECTION 112 REJECTIONS ARE OVERCOME

Claims 20-27, 29, and 30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action asserts that claim 20 is indefinite for reciting "equine GM-CSF". Allegedly, the definition in the specification encompasses all functional equivalents. The remaining claims are rejected for depending from an indefinite claim.

Claims 20, 22, 24-27, 29, and 30 are rejected under 35 U.S.C. §112, first paragraph, because allegedly, the specification is only enabling for horse GM-CSF of SEQ ID NO: 9 or biologically active fragments thereof, but allegedly does not reasonably provide enablement for the full scope of any protein that meets the aforementioned specification definitions of being "equine GM-CSF", including all possible functional equivalents thereof.

Applicants respectfully disagree and traverse the rejections, collectively.

The claims no longer merely recite isolated equine GM-CSF. Rather, the invention as claimed is an isolated polypeptide of equine or synthetic origin which has an adjuvant effect, immunity stimulant activity, and species-specificity as that of equine GM-CSF as set forth in SEQ ID NO:9. That is, "equine GM-CSF" is used in the claims with reference to SEQ ID NO:9, i.e., having the adjuvant effect, immunity stimulant activity, and species specificity of SEQ ID NO:9. Therefore, the Section 112, second paragraph, rejection is overcome.

Further still, the Office Action admits that the application is enabling for SEQ ID NO:9 and biologically active fragments of horse GM-CSF of SEQ ID NO:9; and, the Office Action further notes that claims limited to horse GM-CSF are allowable over the prior art. The Examiner is thanked for these helpful observations. The Examiner's helpful suggestions are met herein by the claims calling for an isolated polypeptide of equine or synthetic origin which has an adjuvant effect, immunity stimulant activity, and species-specificity as that of equine GM-CSF as set forth in SEQ ID NO:9. More in particular, by the recitations of the claims, the polypeptide of the claims has the biological activity of SEQ ID NO:9 - the adjuvant effect, the immunity stimulant effect, and the

species specificity. The claimed polypeptide is clearly that which the Examiner has indicated to be enabled and free of the art.

Indeed, the portions of the application herein cited for the amendments to the claims demonstrates that the application has written description and enablement for the claim recitations and that the claims are indeed free of the art, i.e., that the claims meet that which the Examiner has indicated to be enabled and free of the art.

For instance, at page 2, line 5 the application states: "The administration of heterologous GM-CSF, that is to say obtained from a species other than the one treated, does not make it possible to obtain an optimum adjuvant effect, in particular a stimulation of the activity of the haematopoietic cells and a substantial increase in the immune response." Necessarily, the corollary of this is that the isolated polypeptide of the instant invention has the adjuvant effect, immunity stimulant activity and species-specificity of SEQ ID NO:9 - homologous equine GM-CSF. Attention is also respectfully directed to page 3, line 29 to page 4, line 8 (describing that invention includes polypeptides of equine origin or which are synthetic having substantially equivalent activity to that of natural equine GM-CSF); page 4, lines 11-34 (describing invention as including expression vectors transformed by a sequence according to the invention, and equine GM-CSF proteins thus produced and their use as an adjuvant for vaccines or for stimulating immunity); page 2, line 33 to page 3, line 7 (describing invention as covering equivalent nucleic acid sequences to SEQ ID NO:8, e.g., which differ by the degeneracy of the genetic code, or having 90% or 92% or 95% identity with SEQ ID NO:8, and encode a protein of equivalent functionality and specificity in horses to equine GM-CSF of the invention, e.g., SEQ ID NO:9); page 3, lines 21-25 (describing invention as including equine GM-CSF polypeptide encoded by SEQ ID NO:8 or equivalent sequences). It is respectfully requested that the claims be read in light of the disclosure set forth in the application, including herein cited portions thereof; and, it is noted that when read in the light of the application, the term "equine GM-CSF" is neither indefinite nor non-enabled.

It is respectfully submitted that the reliance in the Office Action upon Hammond, to allegedly show that human GM-CSF has been found to be active on equine dendritic cells, and that therefore, there is cross-species reactivity, is therefore, misplaced.

Hammond relates to the generation *ex vivo* of equine dendritic cells from peripheral blood mononuclear cells (PBMC) using recombinant human GM-CSF and recombinant equine IL-4.

Hammond stands only for the proposition that recombinant human GM-CSF may lead to activation of cells and a differentiation towards macrophages of PBMCs in culture.

Even if human GM-CSF were able to stimulate the differentiation of PBMCs into equine dendritic cells, Hammond provides no guidance or indication that the same would be true *in vivo*.

Indeed, Hammond suggests quite the opposite with the authors' own admissions (*see* page 211, second paragraph of the Discussion) that the numbers of viable equine dendritic cells rapidly declined in culture. Further, the Hammond authors state that: "The inability to culture equine DC for extended periods of time before a decline in cell population numbers may be due to the reliance upon cross-reactive rhGM-CSF and not autologous equine GM-CSF." (end of same paragraph). That is, the data in Hammond shows that there is not the cross-reactivity that is asserted in the Office Action.

Moreover, the Examiner's attention is respectively drawn to Mauel et al., Immunology 117:463-473 (2006) (copy enclosed), citing the method in Hammond as being "far from optimal for obtaining DC and was not reproducible in our hands." (Page 468, first paragraph of the Discussion).

Thus, contrary to assertions in the Office Action, GM-CSF from any other species would NOT provide the same result as natural equine GM-CSF, e.g., SEQ ID NO:9. In other words, it is NOT possible to use GM-CSF of another species (heterologous GM-CSF) in an equine to elicit a sustained stimulation of the activity, and a substantial and sustained increase in the immune response because heterologous GM-CSF, if active in a host, is significantly weaker, with a short duration of activity, and even the possibility of an immune response stimulated against the heterologous GM-CSF; in contrast to the sustained stimulation of the activity of the haematopoietic cells and the substantial increase in the immune response elicited by natural or homologous equine GM-CSF, e.g., SEQ ID NO:9, in a horse. Thus, the requirement of the claims that the claimed polypeptide has an adjuvant effect, immunity stimulant activity, and species-specificity of SEQ ID NO:9 has real meaning in distinguishing the claims from the prior art and in meeting the Examiner's observations for enablement.

Even further still, the application describes how to use the claimed polypeptides, e.g., *see* the Examples. Moreover, Example 2 discloses the use RACE-PCR technique used to isolate the gene encoding the equine GM-CSF. As is known in the art, RACE-PCR can obtain a different nucleic acid molecule than SEQ ID NO:8, and hence a different - but indeed homologous - equine GM-

CSF polypeptide, depending upon the horse sample used for performing the RACE-PCR and the natural variation within homologous equine GM-CSF and DNA coding therefor. Indeed, in this regard, attention is respectfully directed to Mauel enclosed herewith wherein using RACE-PCR an equine GM-CSF with a different sequence than in the present application was obtained. Thus, by Example 2, the skilled artisan is indeed provided with a method for obtaining different homologous equine GM-CSFs that will have the sequence-specificity of SEQ ID NO:9; and, the Applicants are entitled to claims of that breadth.¹ Therefore, one of skill in the art would be able to make and use the isolated polypeptide, i.e., equine GM-CSF, of the present invention without undue experimentation.

In light of the arguments above, Applicants submit that the disclosure in the specification is indeed enabling to make and use the isolated polypeptide, i.e., equine GM-CSF, of the present claims. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first and second paragraphs, are respectfully requested.

REQUEST FOR INTERVIEW PRIOR TO ISSUANCE OF NEXT PAPER

If any issue remains as an impediment to allowance, an interview with the Examiner and the Examiner's SPE are respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview prior to issuing any paper other than a Notice of Allowance.

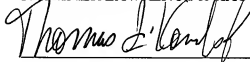
¹ Also submitted herewith is Minke et al., "Use of DNA and recombinant canarypox viral (ALVAC) vectors for equine herpes virus vaccination," Veterinary Immunology and Immunopathology 111:47-57 (2006) wherein there were repeated administration of equine GM-CSF of SEQ ID NO:9 with no observed adverse result, and hence that the equine GM-CSF of SEQ ID NO:9 is also indeed homologous or species-specific (as well as an immunity stimulant having adjuvant effect in the horse).

CONCLUSION

In view of the amendments and remarks herewith and the enclosures herewith, the application is in condition for allowance. Reconsideration and withdrawal of the objections to and rejections of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
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